Age and Incidence of Estrogen Receptor Positive Breast Tumors

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ABSTRACT

Estrogen receptors of primary breast cancer tumors were determined by sedimentation analysis. Positive tumors from pre- and post-menopausal patients were those that contained estrogen receptor content >250 and >750 fmoles per g wet weight tissue, respectively. A positive correlation of patients’ age with increasing incidence of estrogen receptor positive tumors was found; test for linear trend significance z = 5.38 (P < 0.001). One-sixth of those <29 years had positive tumors, 27 percent in the age group 40 to 49 years, 46 percent in those 70 to 79 years, and 62 percent in those 80 years or older.

Introduction

In clinical laboratory practice, measurement of the estrogen receptor implies that only unbound sites in the cytosol are determined. Most investigators would agree that breast tumors from elderly women usually possess a higher estrogen receptor content than those from younger women. This lower receptor content of young women has been attributed by some to their circulating estrogens occupying a portion of the estrogen receptor binding sites. However, no evidence has been offered to substantiate this hypothesis. One detailed study confirmed the presence of a higher unbound estrogen receptor content in those over 55 years but failed to find any obvious difference in the concentration of occupied receptor when comparing tumors from older and younger women.4

Not only do tumors from younger women tend to possess less estrogen receptors, but the receptor content required to elicit a likelihood of response to endocrine intervention is also much lower for pre-menopausal women. DeSombre et al found that endocrine responsive tumors from pre-menopausal women required a minimum receptor content of 250 fmoles per g wet weight tissue whereas a minimum value of 750 fmoles was found necessary for those who were post-menopausal.1

Thus, both age and menopausal status seem to be involved in the biology of the breast cancer tumor.

To understand further the role of age and menopausal status on the estrogen receptors of breast cancer tumors, the
frequency of positive tumors in patients of various age groups was studied.

Patients

The criteria for patient selection were: (1) less than 49 years of age and pre-menopausal and (2) 50 years and older and post-menopausal.

Tumors were considered positive according to DeSombre et al.1

In all, 814 patients with positive tumors were studied: 234 were <49 years and pre-menopausal, and 580 were 50 years or older and post-menopausal.

Patients with positive tumors but who were excluded were four of peri-menopausal status, four who were <49 years and post-menopausal, and six who were >50 years and pre-menopausal.

Method

Estrogen receptor content was measured by sedimentation analysis of sucrose gradients, 10 to 30 percent, in the presence of tritiated estradiol 5 \times 10^{-10}M alone or together with its competitor, diethylstilbestrol 5 \times 10^{-7}M, as previously described.1 Tumor tissue was obtained at operation, stored in liquid nitrogen, and assayed within three days.

Results

The frequency of positive tumors in patients of different age groups are shown in figure 1.

The results show that for pre-menopausal patients there is a small but distinct increase in the frequency of positive tumors that is positively correlated with age; whereas only one-sixth of those less than 29 years of age possessed positive tumors, 25 percent were positive in those older than 40 years. Comparing post-menopausal patients at various age decades, a similar but more pronounced tendency was observed; 25 percent of the patients were estrogen receptor positive in the 50 to 59 year age group while in those over 70 years, 50 percent showed positive tumors. The test for linear trend significance, z = 5.38, P < 0.001.3

Discussion

Two-thirds of the patients with estrogen receptor positive tumors can be expected to respond to endocrine intervention.1 In contrast, less than 10 percent of those with negative tumors respond. Thus, the present study finds that age has a beneficial effect on breast cancer tumor response in that the incidence of estrogen receptor positive tumors increases with age. Whether or not this ageing affect is a reflection of a physiological ageing process is unknown. The few isolated reports on the estrogen receptor content on non-malignant breast tissue suggest that low levels of receptor are found in both pre- and post-menopausal women.

Age as a factor affecting the response
to treatment has not been described in malignancy. Recently, however, ageing was found to improve the response to chemotherapy for gliomas as determined in vitro employing the clonogenic assay. These authors suggested that differences in tumor response may well reflect a normal ageing process. Both the present study on breast cancer and the published findings on gliomas employ in vitro systems. These findings suggest that clinical studies on age as a factor influencing the response to treatment may be clinically valuable.

References


